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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
11/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/557,602	KON ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/15/06 and 10/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 24-42 are pending.

2. Applicant's election without traverse of Group II, claim 2 (now 24-42) drawn to drawn to a method for treatment of diseases caused by activation of immunocompetent cells, characterized in administering the therapeutic agent comprising an antibody to osteopontin or peptide fragment thereof, filed on 9/15/08, is acknowledged.

3. Applicant's IDS, filed 2/15/06 and 10/23/07, is acknowledged, however, references AD, AE, AI, AJ and AK were crossed out because the English translation was not found. Further, references AW-AAJ were crossed out because the entire documents were not found. Applicant is invited to produce such documents.

4. Claim 25 is objected to under 37CFR 1.821(d) for failing to recite the SEQ ID NO for SVVYGLR in the claim.

5. Claim 40 is objected to for misspelling "hapatitis".

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 24-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treatment of autoimmune hepatitis with anti-RGDSVVYGLR antibodies, does not reasonably provide enablement for a method for treatment of diseases caused by activation of imunocompetent cells, comprising administering to a patient in need thereof a therapeutic agent comprising, as the active ingredient, an immunocompetent cell activation inhibitor comprising an antibody to osteopontin or peptide fragment thereof claimed in claim 24-42. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification uses concanavalin A (ConA)-induced hepatitis animal model (Examples 2-3). ConA, a plant lectin and T cell mitogen, rapidly induces severe immune-mediated hepatitis in

mice that is associated with increased TNF-α, IFN-γ, IL-12, IL-18, and IL-4 expression and in which NKT lymphocytes, CD+ T cells, and Kupffer cells have a contributory role (see Margalit et al, Am J. Physiol. Gastrointest. Liver Physiol. 289:G917-G925, 2005). Example 2 of the specification discloses that the ratio of the number of the necrosed cells in the hepatitis tissue (necrosis rate) was about 10% in the liver of the mice administered with M5 antibody, but was about 50% in the liver of the mice administered with rabbit IgG (FIG. 3) On the other hand, the ALT value of the mice administered with M5 antibody was about 1500, and was lower than the value, about 5000, of the control mice (FIG. 1) The results confirm that the M5 antibody inhibits the necrosis of hepatocytes caused by hepatitis. Example 4 discloses that the ALT level of the OPN-deficient mice was lower than that of the wild mice. The survival rate of the OPN-deficient mice was higher (Fig. 6).

Claim 1 recites treating "diseases caused by activation of immunocompetent cells", however, besides autoimmune hepatitis, the specification fails to treat diseases caused by activation of immunocompetent cells. No direction or guidance is provided to assist one skilled in the art in the selection of all such possible diseases caused by activation of immunocompetent cells nor is there evidence provided that all such disease would be treated.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since ConA-induced hepatitis and OPN-deficient animals were used as model system to treat autoimmune hepatitis. It is not clear that reliance on the model data accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively treat a diseases caused by activation of immunocompetent cells such as asthma, arthritis, diabetes, lupus, MS, arteriosclerosis and lung fibrosis or reach any therapeutic endpoint in mammals by administrating the therapeutic composition. The specification does not teach how to extrapolate data obtained from an ConA-induced hepatitis and OPN-deficient studies to the development of effective in vivo mammalian therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the therapeutic package exemplified in the specification.

Demonstrating inhibition of IFN-γ, MIP-2, IL-4, Fas/FasL mediated cell injury cannot alone support the predictability of the method for treating diseases caused by activation of immunocompetent cells through administration of the appropriate formulation. The ability of a host to suppress and thereby treat asthma, arthritis, diabetes, lupus, multiple sclerosis, arteriosclerosis and lung fibrosis will vary depending upon factors such as the condition of the host and burden of disease.

For Example, Blom et al in Science Mag. 299:1845a, 2003 teaches the role for OPN in inflammatory disease is still an open issue. The lack of effect in the OPN-deleted mouse is most likely explained by the influence of other genes that may replace the role of OPN (see last ¶). Blom et al teach that in contrast to the findings published by Chabas et al and others, they saw no effect on any inflammatory model tested-EAE, CIA or CAIA (see table 1 and page 1845a, 1st col., last ¶). Blom et al teach that there are several difficulties in using knockout mice in

providing conclusive evidence for genes in disease traits, like the role of OPN in inflammatory diseases (see page 1845, 3rd col., last ¶). Finally, Blom et al teach the prior art models represent an acute inflammation but are not dependent on T or B cells (see page 1845a, 2nd col., end of top ¶).

It is noted the in Example 2 of the specification, Applicant did not show any efficacy in the ConA-induced hepatitis model treated with anti-OPN antibodies, but rather the rate of necrosis (the ratio of the number of the necrosed cells in the hepatitis tissue).

Finally, it is not clear whether the viral hepatitis and drug-induced hepatitis are represented in Applicant's ConA/OPN-/- animal model. For example, the etiological factor for the autoimmune hepatitis is not known. Each type of hepatitis has its own effective therapy.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 24-39 and 41-42 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/63241.

The `241 publication teaches a method for modulating immune responses in a subject using modulators of Eta-l (early T lymphocyte activation-l)/ostcopontin. The `241 publication teaches methods of treating infections, immune disorders and diseases, autoimmune disorders and diseases, various immunodeficiencics and cancer (see abstract), wherein the autoimmune disorder is chronic active hepatitis (see page53, lines 10-27). The `241 publication claims A method of modulating a type-1 immune response in a subject comprising administering to said subject an Eta-1/osteopontin modulator such that the type-1 immune response is modulated (published claim 1). A method of downregulating a type-1 immune response in a patient comprising: (a) selecting a patient suffering from a disorder that would benefit from a downregulated type-1 immune response: and (b) administering to said patient an Eta-1/osteopontin inhibitory modulator such that the type-1 immune response is downregulated (see published claim 11), wherein the disorder is selected from the group consisting of bacterial arthritis, granulomatous disorder, glomerulonephritis, rheumatoid arthritis, multiple sclerosis, herpes simplex keratitis, and autoimmune disease (diseases caused by activation of immunocompetent cells) (see published claim 12), wherein said Eta-1/osteopontin modulator is an antibody which specifically binds Eta-1/osteopontin (see published claim 42), wherein the

antibody is specific for the *RGD sequence* of Eta-1/osteopontin (e. g., the integrin binding domain) (page 32, line 12-14). The `241 publication teaches that the immune cell being modulated are a macrophage, a dendritic cell, a T cell, a B cell, a monocyte and a neutrophil (immunocompetent cells) (see published claim 20). The publication teaches VVYGLR (e. g., amino acid residues 162-168 of SEQ ID NO : 2), an N-terminal fragment ("Eta-1/opn NT) containing the RGD motif (see page 70, lines 6-10).

Claim 42 is included because the chronic active hepatitis is characterized by necrosis of hepatocytes, a treatment of chronic active hepatitis would lead to inhibition of necrosis of hepatocytes.

The immunocompetent cells being "NKT cells" claimed in claim 29, "inhibits IFN-γ production by the NKT cells" claimed in claim 30, "inhibits MIP-2 production by the NKT cells" claimed in claim 31, "inhibits IL-4 production by the NKT cells" claimed in claim 32, the T cells being "$CD4^+$ T cells" claimed in claim 35, "inhibits Fas/FasL mediated cell injury" claimed in claim 36, "inhibits neutrophil mediated cell injury" claimed in claim 37 is inherent property of the prior art method. Although the reference is silent about these limitation, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

It is reasonable to conclude that the same patient is being administered the same active agent in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method.

The reference teachings anticipate the claim invention.

10. Claims 24-38 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/081522 (IDS reference).

The `522 publication teaches the use of an anti-osteopontin antibody to inhibit the binding of an integrin to osteopontin which inhibits the binding of the integrin recognizing RGD sequence to osteopontin and recognizes SVVYGLR sequence. The `522 publication teaches that the antibody is useful for remedies for autoimmune diseases, rheumatism, rheumatoid arthritis or arthritis

deformans containing any of the anti-osteopontin antibodies as active ingredient (see abstract in particular).

The immunocompetent cells being "NKT cells" claimed in claim 29, "inhibits IFN-γ production by the NKT cells" claimed in claim 30, "inhibits MIP-2 production by the NKT cells" claimed in claim 31, "inhibits IL-4 production by the NKT cells" claimed in claim 32, the T cells being "$CD4^+$ T cells" claimed in claim 35, "inhibits Fas/FasL mediated cell injury" claimed in claim 36, "inhibits neutrophil mediated cell injury" claimed in claim 37 is inherent property of the prior art method. Although the reference is silent about these limitation, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

It is reasonable to conclude that the same patient is being administered the same active agent in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method.

The reference teachings anticipate the claim invention.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/63241 as applied to claims 24-39 and 41-42 above, and further in view of Authur (Autoimmune Liver Disease, 53-56, 2002).

The teachings of the `241 publication has been discussed, supra.

The reference teachings differ from the claimed invention only in the recitation of viral hepatitis.

Arthur teaches that autoimmune hepatitis can present as an acute illness resembling severe acute viral hepatitis (see page 56, under practice points in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the autoimmune hepatitis disease taught by the `241 publication for the viral hepatitis disease taught by Arthur in a treatment method using anti-OPN antibody.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because autoimmune hepatitis present as an acute illness resembling severe acute viral hepatitis as taught by Arthur.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 24-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 36-45 of copending Application No. 11/836,078. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claiming treating rheumatoid arthritis (disease caused by activation of immunocompetent cells) with antibodies that recognized RGD and SVVYGLR.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 24-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-13 of copending Application No. 11/755,671. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claiming treating rheumatoid arthritis (disease caused by activation of immunocompetent cells) with antibodies that recognized RGD and SVVYGLR.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 14, 2008

/Maher M. Haddad/
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